

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

1. (Currently amended) An on-line detection method comprising the on-line coupling of an effluent comprising analytes ~~analyte-containing effluent~~ of a prior fractionation step to a mass spectrometer, which method comprises,

adding a controlled amount of an affinity molecule to an effluent comprising unknown analytes, wherein affinity molecule-analyte complexes form from the affinity molecule with the target analytes in a liquid phase,

performing a first separation step using a restricted-access support, whereby the affinity molecule-analytes complexes permeate the restricted-access support, while smaller molecules than the affinity molecule-analyte complexes are retained,

collecting the affinity molecule-analyte complexes followed by dissociating the affinity molecule-analyte complexes, and

performing a second separation step in which the dissociated target analyte and affinity molecules are each separated, followed by detecting the dissociated target analyte using a mass spectrometer.

2. (Currently amended) On-line detection method according to claim 1, in which the second separation step is carried out using a restricted-access support, in which the affinity molecule is retained, followed by elution of the target analyte from the restricted-access support using a suitable carrier stream, and directing the eluted stream to the mass spectrometer.

3. (Currently amended) On-line detection method according to claim 1, in which the

second separation step is carried out using a hollow fiber support, whereby the target analyte is permeated and the permeate is directed to the mass spectrometer.

4.(Previously presented) On-line detection method according to claim 1, in which the dissociation step is a low pH shock, contacting with a high ionic strength solution, contacting with an organic solvent and/or contacting with a chaotropic reagent.

5.(Previously presented) The method according to claim 1, in which the fractionation step is a liquid chromatography separation, a capillary electrophoresis step or a combinatorial chemistry system, which is optionally followed by a separation step which removes the high molecular weight background.

6. (Previously presented) The method according to claim 5, in which the liquid chromatography separation step is a HPLC, a reversed phase HPLC, a CE, a CEC, a IEF or a MEKC step.

7. (Previously presented) The method according claim 1, in which the mass spectrometer is of the type chosen from the group consisting of electrospray ionization type, atmospheric pressure ionization type, quadrupole type, magnetic sector type, time-off flight type, MS/MS, MSⁿ, FTMS type, ion trap type and combination thereof.

8. (Previously presented) The method according to claim 1, in which the mass spectrometer is set to detect ions of a selected single m/z trace, selected multiple m/z traces, in scanning mode or any sequential mode.

9. (Previously presented) The method according to claim 1, wherein the affinity molecule is an affinity protein.

10. (Previously presented) The method according to claim 1, wherein the affinity molecule is an orphan receptor.

11. (Canceled)

12. (Canceled).